

## Zynyz® (retifanlimab-dlwr) (Intravenous)

Document Number: OHSU HEALTHSERVICES-0700

Last Review Date: 06/05/2025

Date of Origin: 03/31/2023

Dates Reviewed: 04/2023, 09/2023, 12/2023, 03/2024, 07/2024, 10/2024, 01/2025, 04/2025, 06/2025

### I. Length of Authorization <sup>Δ 1,13-15</sup>

Coverage will be provided for 6 months and may be renewed for up to a maximum of 24 months (26 total doses) of therapy, unless otherwise specified.

- Squamous Cell Carcinoma of the Anal Canal in combination with chemotherapy: Coverage will be provided for 6 months and may be renewed for up to a maximum of 12 months (13 total doses).

### II. Dosing Limits

**Max Units (per dose and over time) [HCPCS Unit]:**

- 500 billable units every 4 weeks

### III. Initial Approval Criteria <sup>1</sup>

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

#### **Universal Criteria <sup>1,2</sup>**

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy <sup>Δ</sup>; **AND**
- Used as single agent therapy, unless otherwise specified; **AND**

#### **Squamous Cell Carcinoma of the Anal Canal (SCAC) † ‡ Φ <sup>1-2,9-10,16</sup>**

- Used in combination with carboplatin and paclitaxel for first-line treatment of inoperable locally recurrent or metastatic disease †; **OR**
- Used for locally recurrent disease with progression on or intolerance to platinum-based chemotherapy; **OR**

- Used as subsequent therapy for metastatic disease (if no prior immunotherapy received)

#### **Merkel Cell Carcinoma (MCC) † ‡ Φ<sup>1-4</sup>**

- Patient has metastatic or recurrent locally advanced disease †; **OR**
- Patient has primary locally advanced disease ‡; **AND**
  - Both curative surgery and curative radiation therapy are not feasible; **OR**
- Patient has primary or recurrent regional disease ‡; **AND**
  - Both curative surgery and curative radiation therapy are not feasible

#### **Small Bowel Adenocarcinoma (SBA) ‡<sup>2,13</sup>**

- Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease OR polymerase epsilon/delta (POLE/POLD1) mutation with ultra-hypermuted phenotype [e.g., tumor mutational burden (TMB) >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Patient has advanced or metastatic disease; **OR**
  - Patient has locally unresectable or medically inoperable disease; **AND**
    - Used as primary treatment

#### **Colon Cancer ‡<sup>2,14</sup>**

- Patient has MSI-H/dMMR disease OR POLE/POLD1 mutation with ultra-hypermuted phenotype (e.g., TMB >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used for locally unresectable, medically inoperable, advanced, or metastatic disease

#### **Appendiceal Adenocarcinoma – Colon Cancer ‡<sup>2,14</sup>**

- Patient has MSI-H/dMMR disease OR POLE/POLD1 mutation with ultra-hypermuted phenotype (e.g., TMB >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used for advanced or metastatic disease

#### **Rectal Cancer ‡<sup>2,15</sup>**

- Patient has MSI-H/dMMR disease OR POLE/POLD1 mutation with ultra-hypermuted phenotype (e.g., TMB >50 mut/Mb) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used for advanced or metastatic disease

❖ If confirmed using an FDA approved assay – <http://www.fda.gov/CompanionDiagnostic>

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

## IV. Renewal Criteria <sup>Δ 1,2</sup>

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Duration of authorization has not been exceeded (*refer to Section I*); **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, severe immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis with renal dysfunction, dermatologic adverse reactions/rash, etc.), complications of allogeneic hematopoietic stem cell transplantation (HSCT), solid organ transplant rejection, etc.

<sup>Δ</sup> **Notes:**

- Patients responding to therapy who relapse  $\geq 6$  months after discontinuation due to duration (i.e., receipt of 24 months of therapy) are eligible to re-initiate PD-directed therapy.
- Patients previously presenting with aggressive disease who are exhibiting stable disease on treatment as their best response (or if therapy improved performance status) may be eligible for continued therapy beyond the 24-month limit without interruption or discontinuation.
- Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate PD-directed therapy and will be evaluated on a case-by-case basis

## V. Dosage/Administration <sup>Δ 1,9-15</sup>

Indication	Dose
Squamous Cell Carcinoma of the Anal Canal	<p><u>Combination Therapy:</u></p> <p>Administer 500 mg intravenously every four weeks until disease progression or unacceptable toxicity, or up to 12 months.</p> <p><u>Monotherapy:</u></p> <p>Administer 500 mg intravenously every four weeks until disease progression or unacceptable toxicity, or up to 24 months.</p>
All other indications	Administer 500 mg intravenously every four weeks until disease progression or unacceptable toxicity, or up to 24 months.

## VI. Billing Code/Availability Information

HCPSC Code:

- J9345 – Injection, retifanlimab-dlwr, 1 mg; 1 billable unit = 1 mg

NDC:

- Zynyz 500 mg/20 mL solution in a single-dose vial: 50881-0006-xx

## VII. References

1. Zynyz [package insert]. Wilmington, DE; Incyte Corporation; May 2025. Accessed May 2025.
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## Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm duodenum

ICD-10	ICD-10 Description
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C4A.0	Merkel cell carcinoma of lip
C4A.10	Merkel cell carcinoma of unspecified eyelid, including canthus
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.20	Merkel cell carcinoma of unspecified ear and external auricular canal
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.30	Merkel cell carcinoma of unspecified part of face
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face
C4A.4	Merkel cell carcinoma of scalp and neck
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast

ICD-10	ICD-10 Description
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.60	Merkel cell carcinoma of unspecified upper limb, including shoulder
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.70	Merkel cell carcinoma of unspecified lower limb, including hip
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, unspecified
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C7B.1	Secondary Merkel cell carcinoma
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.821	Personal history of Merkel cell carcinoma

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC